AD_____

Award Number: DAMD17-03-1-0535

TITLE: Chemotherapy-Induced Alopecia and Symptom Distress in Younger and Older Women With Breast Cancer: Intergroup Differences and Impact on Functional Status

PRINCIPAL INVESTIGATOR: Carrie Tompkins Stricker

CONTRACTING ORGANIZATION: University of Pennsylvania
Philadelphia, Pennsylvania 19104-3246

REPORT DATE: August 2004

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	August 2004	Annual Summary (7 July 2003 - 6 July 2004)

4. TITLE AND SUBTITLE
Chemotherapy-Induced Alopecia and Symptom Distress in Younger and Older Women With Breast Cancer: Intergroup Differences and Impact on Functional Status

5. FUNDING NUMBERS
DAMD17-03-1-0535

6. AUTHOR(S)

Carrie Tompkins Stricker

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Pennsylvania
Philadelphia, Pennsylvania 19104-3246

E-Mail: carrie.stricker@uphs.upenn.edu

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. Abstract *(Maximum 200 Words)* *(abstract should contain no proprietary or confidential information)*

Purpose The purpose of this training grant is to facilitate the awardee's development of breast cancer clinical research skills, particularly with respect to older women's symptoms, function, and physical activity during breast cancer treatment and survivorship.
Scope The research training program encompasses both didactic coursework and the conduct of dissertation research within the doctoral program of the University of Pennsylvania School of Nursing, and intensive mentored clinical research experience at the Abramson Cancer Center of the University of Pennsylvania.
Major findings Data analysis in progress.
Progress Nine of 13 required courses have been completed towards the PhD degree, and the PhD qualifying exam was successfully defended. The Research Residency requirement for the Nursing PhD degree has been completed. Two published research presentations were given at international oncology meetings (ASCO, MASCC) related to fatigue and functional status of women undergoing adjuvant chemotherapy for early stage breast cancer. The dissertation research proposal is in progress with defense anticipated 9/04. Training experiences are ongoing, including participation in meetings of the Institutional Review Board & the Cancer Center Clinical Trials Scientific Review and Monitoring Committee.

14. SUBJECT TERMS
breast cancer, aging, chemotherapy, symptom distress, functional status

15. NUMBER OF PAGES
12

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Annual Summary, Introduction and Body:

In this first year of funding for this training grant, I have made significant progress towards achieving my stated objectives as outlined through my approved Statement of Work (S.O.W.).

1) Task 1: Participate in educational activities which extend over the entire award period.

I continue to engage in all of the outlined activities at the University of Pennsylvania (Penn), including ongoing participation in and scholarly presentations at the School of Nursing's Geroscholars seminar held by the Hartford Center for Excellence in Geriatric Nursing Education, the Rena Rowan Breast Cancer Research & Clinical Trials meeting, as well as Grand Rounds and journal clubs within the Abramson Cancer Center at Penn.

I have completed 5 courses, and anticipate completion of 1 additional course by 8/31/04, bringing my total to 9 of a required 13 complete prior to the 2004-5 academic year.

I will now be participating in the Clinical Trials and Translational Research short course in July 2005.

2) *Task 2: Engage in a structured research residency pertaining to the conduct of clinical cancer research.*

I have been attending selected meetings of the Institutional Review Board (IRB) at Penn with my mentor Lynn Schuchter, MD, as well as pertinent Clinical Research Unit meetings within the Cancer Center and university-wide meetings of Penn's Office of Human Research.

A modification to my training plan has become necessary due a hold on my mentor's parent Minoxidil Clinical Trial (MCT). The sponsoring company was purchased by another pharmaceutical company, and the MCT was put on hold in September 2003 after the enrollment of 2 subjects. Research training objectives are now being met through participation in an alternative clinical research study. The MCT is still on hold at the time of this report.

Therefore, I have pursued mentored participation in data collection, management, and analysis for the Abramson Cancer Center trial UPCC 03101: The Pattern, Correlates, and Functional Impact of Anemia, Fatigue, and Nausea and Vomiting in an Adjuvant Treatment Setting for Early Stage Breast Cancer. Like the Minoxidil Clinical Trial, this study also recruits women undergoing adjuvant chemotherapy for breast cancer, and provides an excellent forum to facilitate my goal of investigating issues relevant to older women with breast cancer.

Thus far I have, with guidance, constructed the UPCC 03101 study database, prepared a report for and responded to requests for an internal quality assurance (QA) audit, designed a revised consent form to ensure protection of human subjects' information consistent with HIPAA requirements, and prepared amendments and annual reports for Penn's IRB and Clinical Trials Scientific Review and Monitoring Committee.

In addition, I fulfilled the PhD Research Residency requirement through a mentored semester-long experience analyzing data for UPCC 03101. I presented two posters, both at international oncology meetings, as products of the residency. See "Reportable Outcomes".

Task 3: Participate in subject recruitment, targeting older (≥65) women with breast cancer to ensure adequate representation in the proposed companion pilot study.

I wrote a course paper synthesizing published knowledge of older women's motivations for and barriers to participation in clinical cancer research, as well as conducted and analyzed qualitative interviews investigating these issues with women over the age of 65 years. Insights

learned from this project have been applied to recruitment of older female subjects for UPCC 03101. In case of inadequate recruitment of older subjects, I have negotiated a system for recruiting these subjects with at the Joan Karnell Cancer Center at Pennsylvania Hospital, where a larger proportion of older cancer patients are treated. Due to low numbers of women over 65 years treated with adjuvant chemotherapy, "older women" are now defined as 60 years or older.

With the suspension of the MCT, I will now be unable to recruit subjects for my pilot study through this mechanism. Therefore, I have instead taken on the primary responsibility for oversight of subject recruitment and enrollment for UPCC 03101. I trained a new research coordinator in these responsibilities in January 2004 due to personnel turnover. Enrollment status:

- 72 subjects enrolled during year 1 of funding
- 188 subjects in total accrued since March 2002; target enrollment = 210.
- 24 subjects are 60 years and older. Median age is 49.5 years, range = 25 to 77 years.

Task 4: Develop the design and methods of the proposed pilot study to be conducted in conjunction with the Minoxidil Clinical Trial.
(Note: In my revised S.O.W., this will be replaced by a new Task 4 stating: Develop the design and methods of the dissertation research proposal.)

As noted above, the proposed pilot study can no longer be conducted due to the suspension of the MCT. In order to accomplish the planned objective of designing and carrying out a clinical cancer research study, I am instead developing and conducting my dissertation research as part of my training program. My dissertation research will examine beliefs, attitudes, facilitators, and barriers to physical activity & exercise in older female breast cancer survivors. I plan to submit my dissertation research proposal for IRB review in September 2004. Completion of this task has been delayed due to the change in the study topic due to closure of the MCT.

In addition, a secondary analysis of UPCC 03101 will allow accomplishment of my stated objective to examine differences in symptoms and functional status in older and younger women with breast cancer. Enrollment and data collection for UPCC 03101 are expected to be complete in November 2004, when I will proceed with comparative data analyses.

In the progress of developing the original pilot study design and methods, I wrote both a detailed concept analysis paper on functional status and a comprehensive literature review on functional status in women with breast cancer. In October 2003 I defended the qualifying exam, a state of the science paper synthesizing effects of exercise on functional status and health status in community dwelling older adults. I also wrote a paper applying 3 behavioral theories to the promotion of physical activity in breast cancer survivors, as well as a comprehensive critical review of physical activity measurement in older adults. All these papers were written in the context of PhD coursework in the Schools of Nursing and Public Health.

Task 5: Data Collection for the Pilot Study. *(will read "Data Collection for both UPCC 03101 & the Dissertation Research Study" in the revised S.O.W.)*

- Data collection for UPCC 03101 ongoing as outlined in Task #3.
- Initiation of data collection for dissertation research study anticipated in January 2005.

Task 6: Data Analysis, Pilot Study & Minoxidil Clinical Trial (MCT). *(will read "Data Analysis for both UPCC 03101 and the Dissertation Research Study" in the revised S.O.W.)*

- Data analysis of MCT will not be performed due to discontinuation of study with only 2 subjects enrolled, none of whom proceed to the intervention phase of the trial.

- Ahead of schedule with respect to data analysis of the new parent study, UPCC 03101. Preliminary descriptive, correlational, and inferential analysis have been performed. See Appendix B for abstracts of 2 related posters presented at international meetings.

- Data analysis for the dissertation research study anticipated to begin in June 2005.

Task 7: Prepare and submit manuscripts for publication

- See "Reportable Outcomes" and Appendix B. I also plan to submit my manuscript, "Measurement of Physical Activity in Older Adults", for publication in October 2004.

Key Accomplishments:

1) Completed 5 courses (plus 1 in progress, anticipated completion 8/04) towards 13 required for the PhD degree, for a total of 9 when added to the 3 completed prior to start of funding (see Appendix A).
2) Wrote 6 unpublished manuscripts which meet specific objectives of the training program by synthesizing relevant literature, building argument for the planned study, and providing direction for study methods.
3) Defended the Qualifying Exam in October 2003, a requirement for progression in the doctoral program *(indicated by † in "Reportable Outcomes").*
4) Completed (May 2004) the Research Residency requirement for the Nursing PhD degree.
5) Submitted the Qualifying Exam for presentation at the 57th Annual Scientific Meeting of the Gerontological Society of America; accepted as a paper for presentation on 11/22/04.
6) Presented UPCC 03101 study results at two international meetings – the 2004 annual meeting of the American Society of Clinical Oncology, and the 16th MASCC International Symposium on Supportive Care in Cancer.
7) Appointed member of the Clinical Trials Scientific Review and Monitoring Committee, Abramson Cancer Center of the University of Pennsylvania (May 2004 – ongoing).

Reportable Outcomes:

Publications:

Stricker, C. T., Stein, S. H., & Matthews, G. (2004, June). *Anemia and fatigue during adjuvant chemotherapy for breast cancer: Patterns and impact on quality of life.* Poster discussion session presented at the annual meeting of the American Society of Clinical Oncology, New Orleans, LA.

Stricker, C. T. & Tulman, L. J. (2004, June). *Fatigue during adjuvant breast cancer chemotherapy: Predictors and impact on functional status.* Poster session presented at the 16th International Symposium on Supportive Care in Cancer, Multinational Association for Supportive Care in Cancer, Miami, FL.

Stricker, C. T. (2004, November). *Examination of exercise interventions for older adults: population, function, and health.* Paper to be presented at the 57th Annual Scientific Meeting of the Gerontological Society of America, Washington, D.C.

Unpublished Manuscripts:

Stricker, C. T. (2003). *An evolutionary concept analysis of functional status as it relates to medical and nursing research and care of elders: 1993-2003.* Unpublished manuscript, University of Pennsylvania School of Nursing.

Stricker, C. T. (2003). *Changes in functional status related to adjuvant breast cancer chemotherapy and radiation therapy.* Unpublished manuscript, University of Pennsylvania School of Nursing.

†Stricker, C. T. (2003). *Effect of exercise on functional status and health status in community dwelling older adults: the state of the science.* Unpublished manuscript, University of Pennsylvania School of Nursing. (PhD Qualifying Exam).

Stricker, C. T. (2004). *Participation in breast cancer clinical trials: the older woman's perspective.* Unpublished manuscript, University of Pennsylvania School of Nursing.

Stricker, C. T. (2004). *Increasing physical activity in breast cancer survivors.* Unpublished manuscript, University of Pennsylvania School of Public Health.

Stricker, C. T. (2004). *Measurement of physical activity in older adults.* Unpublished manuscript, University of Pennsylvania School of Nursing.

Awards:

2004 Young Investigator Award, Multinational Association of Supportive Care in Cancer
- awarded at the 16th International Symposium on Supportive Care in Cancer (June 24, 2004)

Research Opportunities:

May 2004 – ongoing:
- Invited member, Breast Cancer Survivorship Study Group of the Living Well After Cancer Program at the Abramson Cancer Center of the University of Pennsylvania
(Angela Demichele, MD; Director & Linda Jacobs, PhD, RN; Coordinator)

APPENDIX A:
Doctoral Coursework

Completed prior to the funding period:

- Nursing 750: Inquiry and Nursing
- Sociology 535: Quantitative Methods in Sociology (Statistics I)
- Nursing 754: Quantitative Research Design and Methods

Completed during the funding period:

- Nursing 753: Evolving Nursing Science
- Nursing 813: Qualitative Paradigm Empirical Nursing Research
- Nursing 816: Health Status, Functional Status, & Quality of Life
- Nursing 800: Dissertation Seminar

In progress:

- Nursing 900: Exercise Physiology & Physical Activity Measurement: Applications to Clinical Research in Older Adults with Cancer

APPENDIX B:

Abstracts of Published Poster & Paper Presentations

Stricker, C. T., Stein, S. H., & Matthews, G. (2004, June). *Anemia and fatigue during adjuvant chemotherapy for breast cancer: Patterns and impact on quality of life.* Poster discussion session presented at the annual meeting of the American Society of Clinical Oncology, New Orleans, LA.

Background: Prior research has failed to delineate a consistent pattern of fatigue and anemia & their impact on quality of life (QOL) during adjuvant breast cancer (BrCA) chemotherapy.
Methods: Study aims: To define the incidence and patterns of anemia and fatigue during and after adjuvant BrCA chemotherapy, & to determine relationships between anemia, fatigue, and QOL. We enrolled 110 patients with Stage I-III BrCA receiving either 4 cycles of Adriamycin & Cytoxan (AC) or AC followed by a taxane for 4 cycles (AC-T). Hemoglobin (Hb) values were obtained on day 1 of each cycle, as well as 6 weeks & 3 months after completion of chemotherapy. Piper Fatigue Scale total scores (PFS) and Linear Analog Scale Assessment (LASA) QOL scores were obtained on day 1 and 8 of cycles 1, 4, 5, and 8 as well as 6 weeks and 3 months following chemotherapy.
Results:
Mean Hb at baseline was 12.9 g/dL, decreased ($p< 0.001$) to 11.7 by Cycle 4 in all patients and Cycle 8 in individuals receiving AC-T. By 3 months post-chemotherapy, Hb recovered to baseline (mean = 12.8).
Fatigue was generally mild (0 - 3) to moderate (4-6) across all cycles of chemotherapy. Mean PFS scores significantly increased over time from cycle 1 [(Cycle 1 day 1 = 2.71) and (Cycle 1 day 8 = 4.07)] to cycle 4 [(day 1 = 3.89 and (day 8 = 5.20)] in all subjects, and from cycle 1 to cycle 8 ([Cycle 8 day 1 = 4.95], and [Cycle 8 day 8 = 5.32]) in all AC-T subjects. Fatigue was significantly worse one week following chemotherapy than on the day of treatment. All results were significant at $p < 0.001$.
Finally, the impact of anemia on fatigue and QOL was explored by categorizing Hb at Cycle 4 into values < 11.5 and ≥ 11.5 g/dl. Although these groups did not significantly differ ($p = 0.19$) on PFS scores, 60% of patients with a Hb < 11.5 had moderate to severe fatigue, as compared to only 46% of those with Hb$\geq$ 11.5 g/dl. Additionally, individuals with Hb < 11.5 had significantly lower QOL on the LASA ($p = 0.011$).
Conclusions: Both anemia & fatigue increase over time across adjuvant BrCA chemotherapy, & fatigue worsens during the week following chemotherapy. In addition, preliminary evidence exists to validate Crawford's (2002) incremental analysis data demonstrating that the most significant increase in quality of life related to hemoglobin occurs between the values of 11 to 12 g/dl.

Stricker, C. T. & Tulman, L. J. (2004, June). *Fatigue during adjuvant breast cancer chemotherapy: Predictors and impact on functional status.* Poster session presented at the 16th International Symposium on Supportive Care in Cancer, Multinational Association for Supportive Care in Cancer, Miami, FL.

Purpose: Fatigue is the most commonly reported symptom by breast cancer patients undergoing adjuvant chemotherapy. However, its predictors and impact on functional status have not been well studied. Study aims were to 1) evaluate predictors of moderate to severe fatigue, and 2) examine its impact on functional status.
Methods: 101 women receiving Adriamycin/Cytoxan (AC) x 4 cycles or AC followed by four cycles of a taxane were evaluated. Fatigue (Piper Fatigue Scale) and symptoms (Symptom Experience Scale) were measured at baseline before chemotherapy, on Day 1 of cycles 2, 4, 5, & 8, and on Day 8 of cycles 1, 4, 5, and 8. Functional status was measured using the Inventory of Functional Status-Cancer and self-reported Karnofsky Performance Scale on Day 1.
Results: The proportion of women with moderate-severe fatigue increased during chemotherapy, from 31% at baseline to 59% at Cycle 8. Baseline age, weight, race, stage, menopausal status, type of surgery, and time since surgery did not predict level of fatigue at any cycle. Baseline fatigue predicted fatigue level at each cycle. The total symptom experience at Day 8 of previous cycles predicted fatigue level at each subsequent cycle, and nausea at previous cycles was the only individual symptom which consistently predicted subsequent fatigue. Women with moderate-severe fatigue had lower functional status across all cycles, and were "just beginning to participate" to "partially participating" in their usual activities, compared to women with none-mild fatigue who were "partially" to "fully" participating. All results were statistically significant.
Conclusions: Women with moderate to severe fatigue had statistically and clinically lower functional status than women with no to mild fatigue. Women with higher baseline fatigue are at increased risk for moderate-severe fatigue during chemotherapy, and should be targeted for intensive fatigue management. In addition, the aggressive management of symptoms, particularly nausea, may also help to ameliorate fatigue during breast cancer chemotherapy.

Stricker, C. T. (2004, November). *Examination of exercise interventions for older adults: population, function, and health.* Paper to be presented at the 57th Annual Scientific Meeting of the Gerontological Society of America, Washington, D.C.

Exercise interventions with community-dwelling older adults have innate appeal to investigators and clinicians who seek to promote health and function. This presentation reports a critical review of the exercise literature in community-dwelling older adults, with an emphasis on isolating discrete populations and functional and health status outcomes. Forty two studies from a MEDLINE search combining "exercise" with "functional status," "health status," and related terms were reviewed. Studies either examined clinical populations of older adults with specific acute/chronic illnesses, or broadly defined non-clinical populations of older adults. Walking or stair-climbing distance or speed improved consistently across both populations. However, improvements in functional status and health status were only seen in non-clinical populations with baseline functional impairments and clinical populations of older adults with symptomatic chronic disease. Improvements in physical functioning of 20-40% were observed with disease-specific measures and the SF-36. Interventions were of higher intensity in sample groups with COPD and osteoarthritis. In healthier older adults, ceiling effects were observed with functional and health status measures. In conclusion, exercise interventions appear to improve functional and health status in clinical populations as well as older adults with early functional decline. Improvement was not seen in healthy populations of older adults. This suggests exercise's utility in correcting functional decline with clinical populations and opportunities for maintenance of functional and health status in those at risk for decline, such as older adults with new onset disease. Clinical populations neglected in current trials, including those with cancer, dementia, and heart failure, are ready for investigation.